PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing (*day/month/year*)	20 JUN 2005
Applicant's or agent's file reference 0180.0076	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US04/42221	16 December 2004 (16.12.2004)	19 December 2003 (19.12.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): C12Q 1/68; A01N 43/04; A61K 31/70 and US Cl.: 435/6; 514/1, 44

Applicant

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1. This opinion contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☒	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Nancy T. Vogel Telephone No. (703) 308-0196

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/42221

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 1-9, 12-15, 17-19	YES
	Claims 10, 11	NO
Inventive step (IS)	Claims 1-9, 12-15, 17-19	YES
	Claims 10, 11	NO
Industrial applicability (IA)	Claims 1-15, 17-19	YES
	Claims NONE	NO

2. Citations and explanations:

Claims 10 and 11 lack novelty under PCT Article 33(2) as being anticipated by Roy et al. (US Patent 6,489,163). Roy et al. disclose a method of inhibiting the growth of prostate cancer cells comprising decreasing the biological function of androgen receptors, by affecting the androgen mRNA levels (see abstract, claims, columns 1-2).

Claims 1-9, 12-15 and 17-19 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a method of determining the physiological effect of a compound on prostate cancer cell, comprising determining whether a level of mRNA encoding the androgen receptor in a prostate cancer cell is at least two fold higher than the level of mRNA in a normal prostate cell, contacting a compound to be tested with said prostate cancer cell having at least two fold higher androgen receptor mRNA than normal prostate cell, and examining the effect of the compound; a method of inhibiting the growth of hormone refractory prostate cancer cells wherein the androgen receptor protein level is decreased through modulation of signal transduction pathways such as targeting EGF receptors that crosstalk to the androgen receptor, or by induction of cellular degradation pathways; or by dissociating the androgen receptor from heat shock proteins; or by using androgen receptor antisense or mRNA knockdown technology; or by modifying the androgen receptor sequence or by posttranslational modifications; or a method of determining if a selected prostate cancer cell is hormone sensitive or refractory, comprising determining the level of mRNA in the cell that encodes androgen receptor polypeptide, and comparing it to said mRNA level in a hormone sensitive prostate cancer cell, and determining whether the selected prostate cancer cell has at least two fold higher level of androgen receptor mRNA than the hormone sensitive cell.

Claims 1-15 and 17-19 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

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Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

There is no claim 16.

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 5-9, 12-15 and 17 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because of the claims not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because: the specification does not provide adequate guidance in order to enable one to practice the claimed invention, since one would not know which mRNA level to measure in any particular mammalian cancer cell, other than prostate cancer cell, in order to carry out the method of claims 5-9; the disclosure does not provide guidance for how to affect androgen receptor protein level through modulation of signal transduction pathways , or by induction of cellular degradation pathways, or dissociation of the androgen receptor from heat shock proteins, or by antisense of knockdown technology, or by modification of the polynucleotide or polypeptide sequence of the androgen receptor, or by posttranslational modifications thereof.